

Four bovine meningeal tumors

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Abstract

Four bovine meningeal tumors from a total of 14 brain tumors were recorded in the files of the Ontario Veterinary College and the Ontario Veterinary Laboratory Services Branch from the years 1966 to 1984. The affected cattle ranged in age from 10 months to adult. They exhibited various nervous signs and, in each case, the animals became recumbent. Tumors were located in various areas of the central nervous system. Neoplastic cells had oval vesicular nuclei containing numerous cytoplasmic invaginations. Virus particles were not observed. A fibroblastic appearance, with the presence of loose whorls or bundles, was present in all. Three of the tumors were invasive and were classified as a fibroblastic meningioma.

Résumé

Quatre cas de tumeurs des méninges chez des bovins

Quatre cas de tumeurs des méninges sur un total de 14 tumeurs du cerveau chez les bovins ont été inscrits aux dossiers de l'«Ontario Veterinary College» et de l'«Ontario Veterinary Laboratory Services Branch» entre les années 1966 et 1984. L'âge des animaux s'échelonnait entre 10 mois et l'âge adulte. Les animaux ont démontré différents signes neurologiques menant dans tous les cas au décubitus. Les tumeurs étaient situées dans différentes régions du système nerveux central. Les cellules néoplasiques avaient des noyaux vésiculaires ovales renfermant plusieurs invaginations cytoplasmiques. Aucune particule virale ne fut observée. Tous les cas avaient une apparence fibroblastique avec présence de spirales ou de faisceaux. Trois des tumeurs étaient infiltrantes et ont été classifiées comme des méningio-sarcomes. L'autre a été classifiée étant un méningiome fibroblastique.

(Traduit par Dr Thérèse Lanthier)

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Introduction

Meningeal tumors are among the most frequent intracranial neoplasms of animals, but are rarely reported in cattle (1-7). Primary intracranial tumors are reported infrequently in cattle (1,2,4,5,7,8), although astrocytomas (6), gliomas (6), ependymomas (6,7), schwannomas (9), oligodendrogliomas (6), and medulloblastomas (10,11) have been recorded.

A very high prevalence of meningiomas is found in aged cats (12,13) and a relatively high prevalence has been reported in dogs, particularly in the German Shepherd and Collie breeds (6). In man, meningiomas account for 15-20% of all intracranial tumors in adults, but are much less frequent in children (14,15).

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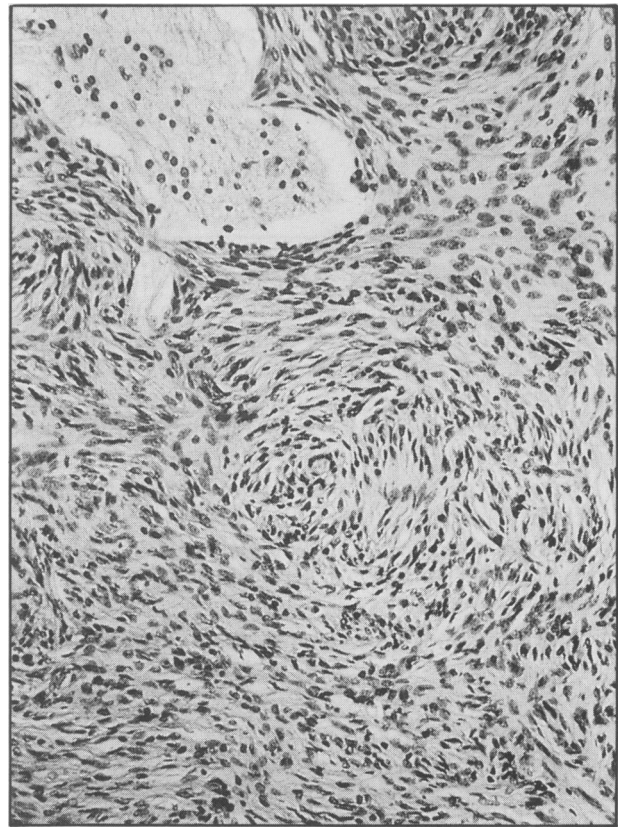


Figure 1. Fibroblastic tumor cells arranged in a swirling pattern in the meningeal sarcoma in case 1. H&E.

Occasionally, highly malignant meningeal sarcomas occur in children or young adults (14).

Bovine meningiomas have been recorded as primary tumors (16) and as an incidental finding in a cow with cerebral cysticercosis (17).

Materials and methods

Four meningeal tumors were identified in a search which revealed 14 bovine central nervous system (CNS) tumors in the files of the Department of Pathology, Ontario Veterinary College (OVC) (1966-1984) and the Veterinary Laboratory Services Branch, Ontario Ministry of Agriculture & Food (VLS) (1969-1984). Two of the meningeal tumors were referrals, one from Manitoba and one from New Brunswick. In all cases, representative neoplastic tissue had been fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned at 6 μ m, and stained with hematoxylin and eosin. Formalin-fixed, paraffin-embedded tissue was available in one case and reticulin stains (Gordon-Sweet) as well as immunoperoxidase stains for glial fibrillary acidic protein (GFAP) were used. This tissue was also used to obtain semi-thin (1 μ m) sections which were stained with methylene blue and examined by light microscopy; ultrathin sections of selected areas were stained with lead citrate and uranyl acetate and examined in a Hitachi transmission electron microscope, model H39.

Table 1. Clinical findings in four cattle with meningeal tumors

Case	Age	Clinical signs	Tumor characteristics	Tumor location
1	24 mo	staggering, opisthotonos, blindness, recumbency	2 cm, oval, firm	left rostroventral cerebrum
2	8 mo	blindness, progressive neurological deterioration, recumbency	2-3 cm	septal nucleus
3	adult	head pressing, nystagmus, recumbency	3 × 5 cm, white	left occipital lobe
4	10 mo	stilted gait, recumbency	multiple 2-10 mm nodules	ventral, from medulla oblongata to thoracic spinal cord

Results

Several days after delivering her first calf, a two-year-old Holstein cow exhibited nervous signs consisting of staggering and head elevation. Her condition deteriorated over a period of one week, leading to recumbency, opisthotonos, and blindness. On postmortem examination, a firm 2 cm oval mass was noted on the rostroventral aspect of the left cerebrum (Table 1).

On histological examination, this superficial plaque-like mass had interdigitating projections extending deeply into the parenchyma of the brain. The tumor mass was composed of syncytial-appearing cells without definable cell membranes. This resulted in a seemingly continuous, slightly fibrillar eosinophilic background. Cells were occasionally arranged in a swirling pattern or formed loose bundles and whorls (Figure 1). Nuclei were uniformly oval, lacked conspicuous nucleoli and possessed a delicate pattern of chromatin which was often concentrated adjacent to the nuclear membrane. Intranuclear inclusions were common. Mitotic figures were not observed. Deeper in the parenchyma, there was a gradual transition to spindle-shaped cells that formed finger-like, interdigitating projections or prominent perivascular aggregates. Small numbers of lymphocytes and plasma cells infiltrated the entire tumor. Collagen and reticulin stains showed the extensive nature of the parenchymatous involvement. The reaction in the neuropil was severe, consisting of edema and diffuse gliosis, along with large numbers of hypertrophied astrocytes and dense fibrillary cell processes.

Glial fibrillary acidic protein stains were negative within the tumor mass, but were strongly positive for the reactive astrocytes.

Electron microscopy revealed the presence of numerous intranuclear invaginations of cytoplasm. While in most cases these appeared as inclusions surrounded by a clearly defined membrane, direct communication with the cytoplasm was evident occasionally (Figure 2). Viral particles were not observed. Nuclear chromatin was scanty and often margined.

Although the individual cell features appeared benign, the infiltrative pattern of growth supported a diagnosis of meningeal sarcoma.

The clinical course in all four cases ended in recumbency (Table 1).

The appearance of a large syncytium of cells enmeshed in a monotonous background of slightly fibrillar, eosinophilic stroma was a feature in all four tumors examined (Table 2).

In animal 2, even though the tumor mass was well circumscribed, an occasional neuron completely surrounded by neoplastic cells was visible near the periphery of the tumor (Figure 3). Electron microscopic examination revealed intranuclear cytoplasmic invaginations with vesicular nuclei and margined chromatin. There were numerous, irregular, coalescing and sometimes centrally mineralized foci of necrosis.

In case 3, the tumor was well demarcated from the neuropil. Tissue response was minimal, though very little nontumor tissue was available for examination.

Initial examination of cerebrospinal fluid in animal 4 revealed 6×10^6 leukocytes/L and a 2+ reaction to a Pandy test for gammaglobulin. Prior to euthanasia, the Pandy test reaction was 5+. Histologically, neoplastic tissue was composed of plaques of cells that were firmly adherent to the dura mater with focal invasion into the ventral nerve radicles. Demyelination and Wallerian degeneration were present in sections of cord and spinal radicles.

Discussion

Meningeal tumors are derived from cells of the arachnoid membrane (18,19), which share with mesothelial and synovial cells the unique function of acting as epithelium in that they cover a surface or line a cavity (19). In the outer zone of the arachnoid, the cells are more closely packed and function as epithelium. In the deeper layers however, the intercellular connections are looser, and fibroblastic septa are noted between the pia and the arachnoid (19). It is not surprising then to see a mixture of meningotheial and fibroblastic elements in meningeal tumors, often with no sharp demarcation between them. The term transitional meningioma has been applied to these types of tumors.

Controversy still exists concerning whether the meninges are mesodermal or neuroectodermal in origin. There is general agreement that, in early embryological development, a layer of mesenchymal tissue surrounds the developing neural tube, and later condenses to form the covering of the brain and spinal cord. The controversy concerns the participation of neural crest cells in the formation of these primitive meninges (19). In tumors examined in this study and from a review of the literature, there is no evidence for transformation of meningeal tumors to tumors with a neuronal or glial cell component. Rather, all meningiomas, with their variations, seem to follow mesenchymal lines (19).

Meningeal tumors are rarely diagnosed in cattle. The small number found in a survey of 19 years of accessions attests to this. The fact that some were undiagnosed is perhaps not unexpected, due to the cellular variation that occurs between and within individual meningial tumors.

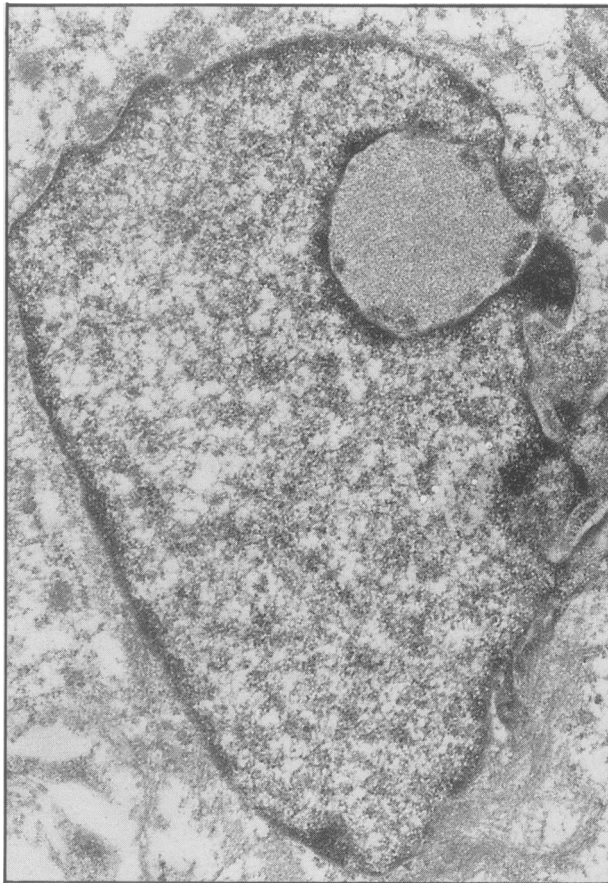


Figure 2. Intranuclear cytoplasmic invagination. The connection to the surrounding neuropil is still clear. Case 1.

The great variety of neural tumors, arising as they do from an organ of great cellular complexity, has created diagnostic problems which have been overcome by the development of various diagnostic techniques. The use of special staining techniques, e.g. reticulin and collagen stains, and the use of the electron microscope help in the diagnosis of meningeal tumors. The latest advance is the application of immunohistochemical techniques. Stains such as GFAP for astrocytes (normal, reactive or neoplastic), galactocerebroside and carbonic anhydrase for oligodendrocytes, and S-100 protein, which is specific for schwannomas, are much superior to conventional stains in specificity (accuracy) and sensitivity (20).

Neurological signs leading to eventual recumbency were manifested in all four animals in this study. In humans, most of the clinical symptoms are caused by local effects of the tumor mass as it exerts pressure on the surrounding tissues with resulting damage to the parenchyma. The neuropil reaction in cases 1 and 4 was marked, no doubt contributing to the progressively deteriorating neurological condition of these animals, but comments cannot be made in cases 2 and 3 due to the minimal amount of brain available for examination.

Although the number examined is too small to generalize, all cases were female animals, and three of the four animals were under two years of age. Meningeal tumors from these three also exhibited qualities of invasiveness, one of the hallmarks of malignancy, and could therefore be classified as meningeal sarcomas.

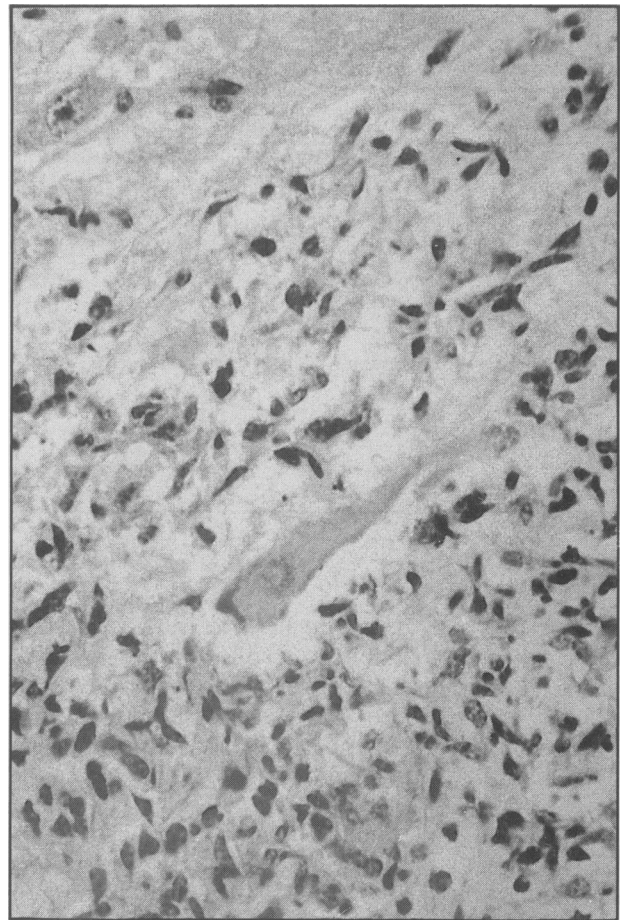


Figure 3. A neuron surrounded by tumor cells in the meningeal sarcoma in case 2. H&E.

This is in spite of the fact that meningeal tumors grow expansively, and compress but rarely invade the brain. Although the relationship to age and sex noted here corresponds to the findings in surveys of human meningiomas, similar results have not been observed in veterinary pathology in other species (12,16).

Causes of meningeal tumors are uncertain. Trauma has been implicated in humans (21). An association of papillomaviruses with malignant tumors in man has become more and more evident (21). Papillomavirus particles, however, have never been observed in malignant carcinomas that are considered to develop from papillomas (21). Meningiomas have been observed in young cats affected with the metabolic disorder, mucopolysaccharidosis I (22). Experimentally, chemical carcinogens (23) and Rous sarcoma virus (24) have induced meningiomas in dogs. There are no reports of naturally occurring virus-induced tumors of the CNS in cattle (25), although intracranial meningeal fibromas have been produced in susceptible calves by inoculation of bovine papilloma virus (BPV) onto the scarified meningeal surface (25). Although a large number of BPV genome equivalents per cell were detected in tumor DNA in artificially induced meningiomas, particles resembling papovaviruses were not seen (26). Virus particles were not observed in sections of the two tumors that were examined by electron microscopy in this study.

The presence of numerous intranuclear cytoplasmic invaginations was demonstrated by electron micro-

Table 2. Comparison of histological features of four bovine meningeal tumors

Case	Invasive- ness	Intranuclear inclusions	Fibroblastic appearance	Necrosis	Mineral	Diagnosis
1	++	++	+++	—	—	meningeal sarcoma
2	+	++	+	+++	+++	meningeal sarcoma
3	—	++	+	++	—	fibroblastic meningioma
4	+	+	+++	—	—	meningeal sarcoma

— not evident
+ mild
++ moderate
+++ marked

scopy. While not confined to meningiomas, the frequent occurrence of intranuclear cytoplasmic invaginations is a feature of human meningiomas (27) and has been noted in BPV-induced meningeal tumors (25). Similarly, tonofilaments, noted within the cytoplasm in cases 1 and 2, are characteristic of human meningiomas (19,27). In the ultrastructural diagnosis of meningiomas, special emphasis is placed on the presence of these structures (19,24).

The intricate and complex interdigitation of cell membranes, another ultrastructural characteristic of meningiomas (19,24), could not be demonstrated in cases 1 or 2 with electron microscopic examination because of the cellular disruption that occurred during tissue processing.

A literature review revealed only six cases of spontaneously occurring meningiomas in cattle (1,2,5-8, 16,17) with one being recorded as an incidental finding (17). Meningeal tumors are comparatively rare in cattle and our survey does little to change that impression.

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